

REMARKS

Status of the claims

Claims 1-25 are pending and claims 1-8 are under consideration in this application, claims 9-25 having been withdrawn from consideration for allegedly being drawn to separate inventions. All the claims under consideration stand rejected. Applicants respectfully request that the minor amendments made herein merely for enhancing clarity be entered. If the amendments are entered, after entry, claims 1-25 will be pending and claims 1-8 will be under consideration in this application.

35 U.S.C. § 103(a) rejections

(a) Claims 1-4, 6, and 7 stand rejected as allegedly being unpatentable over Vijg et al. (the '176 patent), taken in view of *In re Venner*. Applicants respectfully traverse the rejection.

From the comments on page 2, line 26, to page 4, line 2, of the Office Action, Applicants understand the Examiner's position to be that: (i) the '176 patent discloses generating a two dimensional electrophoretic pattern from nucleotide sequence information; and (ii) the method of the instant claims is a mere automation of a prior art manual method. Applicants strongly disagree with this position.

First, in asserting that the '176 patent does disclose the use of nucleotide sequence information, the Office Action actually highlights a core difference between the present invention and the prior art method. Thus the Office Action states: "Vijg et al. utilizes sequence information as part of analyzing 2-D electrophoretic patterns" (emphasis added; page 3, lines 1-2). Thus, the prior art method used sequence information to analyze already generated 2-D electrophoretic patterns made by physically electrophoresing actual DNA in two dimensions on an electrophoretic gel, and not to make a 2-D electrophoresis pattern. In the '176 patent, making the 2-D electrophoresis pattern did not involve the use DNA sequence information. It merely involved physically manipulating the DNA.

In contrast, the method of the invention involves using a computer (as amply disclosed on pages 18-22 of the instant specification) to produce, using genomic sequence information, a computer-stored 2-D electrophoretic pattern containing computer-stored "spots" defined by appropriate 2-D coordinates.

For the same reason, the statement in the Office Action (page 3, lines 11-13) that "relating of spots to restriction fragments, for example, in the reference is reasonably a type of 'deduced by' practice directed to pattern production" is not correct. Here, as above, "relating of spots to restriction fragments" is analyzing an already created 2-D electrophoretic pattern and is not producing or making a 2-D electrophoresis pattern as specified by the instant claims.

For these reasons alone, the method of the instant invention is fundamentally different from, and is thus not rendered obvious by, the '176 patent, in view of *In re Venner* (see below) or not. However, in order only to further clarify claim 1, the term "virtual" has been added immediately after "control" in line 2. From the text of the instant specification (e.g., the last paragraph on page 18 to page 22, paragraph) it is clear that the control 2-D electrophoresis pattern is a "virtual" 2-D electrophoresis pattern. The first step of claim 1 contains an additional amendment, also made in the interest only of increased clarity.

In that making a control 2-D electrophoresis pattern from genomic sequence information is fundamentally different from using sequence information to analyze a 2-D electrophoresis pattern, the claimed method cannot by any stretch of the imagination be considered a mere automation of previously known manual method, a step that *In re Venner* (262 F.2d 91 91 (CCPA 1958)) precludes from endowing patentability. As pointed out in the Amendment and Response filed on June 9, 2004, the only novelty in the apparatus claimed in the patent at issue in *In re Venner* (the "Venner patent") was a timer (set by an operator) to automatically open a particular type of die mold at a critical time. The automatic opening of molds similar to that used in the Venner patent by timers was previously known and manual opening of the type of mold used in the Venner patent at a critical time was also known. The invention merely involved combining these two extremely closely related prior art apparatuses. *Id.*, at 93-95.

Clearly this not the situation here. Thus, for example, there is no teaching in the cited art of using nucleotide information to produce a control 2-D electrophoresis pattern for any purpose, let alone for comparison to a 2-D electrophoresis pattern made by actually electrophoresing actual DNA in two dimensions. The only use of nucleotide sequence information that the '176 could remotely be considered as disclosing is its use for analyzing already made 2-D electrophoresis patterns. Thus, there is no similarity at all between the way the prior art 2-D electrophoresis gel is made and the way the control 2-D electrophoresis gel of the instant claim is made. Therefore, Applicants respectfully submit that the holding of *In re Venner* is not relevant to the instant claims.

(b) Claims 1-8 stand rejected as allegedly being unpatentable over Vijg et al. (the '176 patent), taken in view of *In re Venner*, and further in view of Stevens et al. (the '767 patent).

From the comments on page 4, line 7, to page 5, line 3, of the Office Action, Applicants understand the Examiner's position to be that the '767 patent, in combination with the cited art described above, renders claims 5 and 8 obvious. Applicants strongly disagree with this position for the reasons given below. In addition, the Office Action asserts that, in the Amendment and Response filed June 9, 2004, Applicants merely alleged that the '767 patent lacks support for limitations the Examiner had stated to be disclosed by the '767 (Office Action, page 4, lines 17-20). Applicants did not intend in the prior Amendment and Response to deny what the Examiner had indicated to be disclosed by the '767 patent. Applicants pointed out in the prior Amendment and Response (page 10, lines 1-13), and more explicitly below, why the disclosure of the '767 patent is not sufficient to render instant claims 5 and 8 obvious.

First, in that claim 1 (for the reasons given above) is not rendered obvious in view of the '176 patent and *In re Venner*, claims dependent on claim 1 (including claims 5 and 8) are also not rendered obvious by the two references. Moreover, in that the '767 patent merely discloses a networked system in which a plurality of nucleic acid sequencing machines are linked to a central computer, it does not provide what is missing from the '767 patent in regard to instant

claim 1. Thus, even when the '767 patent is combined with the '176 patent, the combination does not render claim 1 (or any claims dependent on it, including claims 5 and 8) obvious.

However, even if '176 patent and *In re Venner* did render claims 1 obvious, as pointed out in the Amendment and Response filed June 9, 2004, claims 5 and 8 specify embodiments of the invention that would not be rendered obvious by combining these two references with the '767 patent.

Thus, with respect to claim 5, while the '767 patent discloses the above-described network in which sequence information is sent from sequencing machines to a central computer, it does not disclose or contain the slightest suggestion of obtaining sequence information from a genetic sequence database for any purpose, let alone for the purpose of generating the control 2-D electrophoresis pattern, as required by claim 5. Thus, contrary to what the instant Office Action (page 4, lines 10-20) and the Office Action mailed March 11, 2004, state, the '767 patent does not disclose or remotely suggest the type of the "communication line network" specified by claim 5, which the Examiner acknowledges is not disclosed by the '176 application (Office Action of March 11, 2004, page 4, lines 1-3); it is not sufficient that the '767 patent discloses "summariz[ing] the sequencing of DNA and the communication of such information over a network . . . [and] the massive sequence data buildup in the art, especially motivated by disease detection." (Office Action of March 11, 2004, page 4, lines 4-8). Thus, even if the combination of '176 patent and *In re Venner* rendered claim 1 obvious and the two references were combined with the '767 patent, the resulting combination would not disclose all the elements of claim 5, as required for an obviousness rejection involving a combination of references.

Furthermore, even if all the elements of claim 5 were disclosed by the '176 and the '767 patents, neither of the patents contains the required motivation to combine their respective disclosures. Thus, the '176 patent discloses 2-D electrophoretic methods involving actual physical manipulation of DNA for analyzing variations in a large number of genetic loci (e.g., Abstract) and does not disclose or remotely suggest the desirability of transmitting sequence information from even a single sequencing machine, let alone correlating sequence information from a plurality of such machines (as disclosed by the '767 patent). In contrast, while the '767

patent discloses methods of correlating sequence information from a plurality of nucleic acid sequencing machines, it does not mention analyzing multiple genetic loci by any means, let alone doing so by 2-D electrophoresis (as disclosed by the '176 patent). Thus, one ordinarily skilled in the art would not be motivated by either to combine the disclosure of the '176 and '767 patents.

In summary: (a) because the '176 and '767 patents in combination do not render claim 1 obvious, they cannot render claim 5 obvious; (b) even if the two cited patents did render claim 1 obvious, because they do not disclose all elements of claim 5, they could not render claim 5 obvious; and (c) even if the two cited patents did render claim 1 obvious, and together they disclosed all elements of claim 5, because neither contains the required motivation to combine their respective disclosures, they could not render claim 5 obvious

The disclosure of the '767 patent is summarized above. In that the '767 patent does not disclose, or even suggest in the slightest way, memorizing abnormal information (i.e., unidentified nucleotides in the genomic nucleotide sequence, as the term is defined in the instant application; page 19, lines 5-16) detected by a program in genomic nucleotide sequence information at all, let alone memorizing the abnormal information by linking it to a spot in a control produced two-dimensional pattern, as required by claim 8. Thus, contrary to what the instant Office Action (page 4, lines 10-20) and the Office Action mailed March 11, 2004, state, the '767 patent does not come close to disclosing or even suggesting the embodiments specified by claim 5, which the Examiner acknowledges are not disclosed by the '176 application (Office Action of March 11, 2004, page 4, lines 1-3); it is not sufficient that the '767 patent discloses "memorization of sequence data" (Office Action of March 11, 2004, page 4, lines 4-8). Thus, even if the combination of '176 patent and *In re Venner* rendered claim 1 obvious and the two references were combined with the '767 patent, the resulting combination would not disclose all the elements of claim 8, as required for an obviousness rejection.

Furthermore, even if all the elements of claim 8 were disclosed by the '176 and the '767 patents, for the reasons given above, neither of the patents contains the necessary motivation to combine their respective disclosures, which is also required for an obvious rejection based on more than one reference.

In summary: (a) because the '176 and '767 patents in combination do not render claim 1 obvious, they cannot render claim 8 obvious; (b) even if the two cited patents did render claim 1 obvious, because they do not disclose all elements of claim 8, they could not render claim 8 obvious; and (c) even if the two cited patents did render claim 1 obvious, and together they disclosed all elements of claim 8, because neither contains the required motivation to combine their respective disclosures, they could not render claim 8 obvious.

In light of all the above considerations, Applicants respectfully submit that none of claims 1-8 are rendered obvious by the cited art and therefore request that the rejection under 35 U.S.C. §103(a) be withdrawn.

Applicant : Shigeo Yoshida et al.
Serial No. : 10/003,446
Filed : October 26, 2001
Page : 13 of 13

Attorney's Docket No.: 11283-015001 / PH-1269US

CONCLUSION

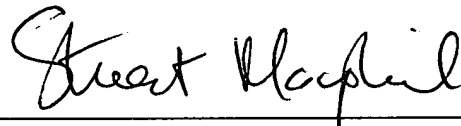
In summary, for the reasons set forth above, Applicants maintain that the pending claims patentably define the invention. Applicants request that the Examiner reconsider the rejections as set forth in the Office Action, and permit the pending claims to pass to allowance.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicants' undersigned representative can be reached at the telephone number listed above.

Enclosed is a request for an automatic extension of time and a check in payment of the extension in time. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 11283-015001.

Respectfully submitted,

Date: 5/24/05



Stuart Macphail, Ph.D., J.D.
Reg. No. 44,217

Fish & Richardson P.C.
Citigroup Center
52nd Floor
153 East 53rd Street
New York, New York 10022-4611
Telephone: (212) 765-5070
Facsimile: (212) 258-2291